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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/057,646	01/25/2002	Harry R. Davis	CV01379K	3480
24265	7590	05/10/2005	EXAMINER	
SCHERING-PLOUGH CORPORATION PATENT DEPARTMENT (K-6-1, 1990) 2000 GALLOPING HILL ROAD KENILWORTH, NJ 07033-0530			WANG, SHENGJUN	
			ART UNIT	PAPER NUMBER
			1617	

DATE MAILED: 05/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/057,646

Applicant(s)

DAVIS ET AL.

Examiner

Shengjun Wang

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 January 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4,7-30 and 32 is/are pending in the application.
- 4a) Of the above claim(s) 11-27 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4,7-10,28-30 and 32 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____

DETAILED ACTION

Receipt of applicants' amendments and remarks submitted January 11, 2005 is acknowledged.

1. The terminal disclaimer filed on January 11, 2005 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of 10/639900 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Claim Rejections 35 U.S.C. 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. Claims 1-4, 7-10, 28-30, 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rosenblum et al. (US 5,846,966, IDS), in view of Kim (US 5,698,527, IDS) and Keller et al (WO 00/38725, IDS).

3. Rosenblum teaches the instant cholesterol absorption inhibitors and its application for lowering serum cholesterol. Rosenblum further teaches that the cholesterol absorption inhibitors may be employed in combination with other cholesterol lowering agents, such as simvastatin. See, particularly, the abstract, and the claims. Rosenblum et al. teach that daily dosage of the compounds is about 5mg to 1000 mg, given in a single dose or 2-4 divided doses. When used in combination with other drug the dose is about 1mg to 1000 mg a dose given 1 or 2 times a day. The exact dose would depend on various conditions. See, particularly, col. 21, lines 17-63.

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4. Rosenblum et al. do not teach expressly a combination of the cholesterol absorption inhibitor and nicotinic acid.

5. However, Kim teaches that nicotinic acid (niacin) is a well-known cholesterol lowering agents, and is particularly useful in combination with cholesterol absorption inhibitors. See, particularly, the abstract, and column 32, lines 9-25. Keller et al. teaches various combinations of cholesterol lowering agents, including ezetimibe and nicotinic acid, for treating hypercholesterolemia-associated disorders. See, particularly, the abstract, and pages 11-14.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to make a composition comprising ezetimibe and nicotinic acid, and optionally simvastatin.

A person of ordinary skill in the art would have been motivated to make a composition comprising ezetimibe and nicotinic acid, and optionally simvastatin because it is prima facie obvious to combine two compositions each of which is taught in the prior art to be useful for same purpose in order to form third composition that is to be used for very the same purpose; idea of combining them flows logically from their having been individually taught in prior art; thus, the claimed invention which is a combination of two known cholesterol lowering sets forth prima facie obvious subject matter. See In re Kerkhoven, 205 USPQ 1069. Further, the prior art have suggested the usefulness of combination of different cholesterol lowering agents, particularly, cholesterol absorption inhibitor and nicotinic acid. As to the specific amount of ezetimibe, note the amount (10 mg) is within the range disclosed by Rosenblum et al. In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a prima facie case of obviousness exists. In re Wertheim, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); In re

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Woodruff, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990). Further, Optimization Within Prior Art Conditions or Through Routine Experimentation Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Response to the Arguments

Applicants' remarks submitted January 11, 2005 have been fully considered, but are not persuasive with respect to the rejections set forth above.

6. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

7. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The prior arts as a whole have fairly suggested the combination of nicotinic acid and ezatimibe. Particularly, both nicotinic acid

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and ezetimibe are known to be useful for treating hypercholesterolemia, and it was known in the art to combine nicotinic acid with cholesterol absorption inhibitor, and ezetimibe is a well-known cholesterol absorption inhibitors. A prima face case of obviousness for the combination has been established. As to the particular amount of ezetimibe (10 mg) herein employed. It is noted 10 mg is within the range disclosed by Rosenblum (1 to 1000 mg). Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical.

"[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Objective evidences herein are not sufficient to rebut the prima facie case of obviousness. The evidences herein merely showing an additive effect of the two individual components would have been reasonably expected. Regarding the establishment of unexpected results, a few notable principles are well settled. It is applicant's burden to explain any proffered data and establish how any results therein should be taken to be unexpected and significant. See MPEP 716.02 (b). The claims must be commensurate in the scope with any evidence of unexpected results. See MPEP 716.02 (d). Further, A DECLARATION UNDER 37 CFR 1.132 must compare the claimed subject matter with the closest prior art in order to be effective to rebut a prima facie case of obviousness. See, MPEP 716.02 (e). Whether a product has been commercialized is not a sufficient evidence for unexpected results. Further, the commercial success of ZETIA (ezetimibe) is not relevant to the issue. The claimed invention is a combination.

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8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shengjun Wang whose telephone number is (571) 272-0632. The examiner can normally be reached on Monday to Friday from 7:00 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SHENGJUN WANG
PRIMARY EXAMINER

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~~SHENGJUN WANG~~
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Shengjun Wang
Primary Examiner
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